REMARKS

Applicant is gratified by the Examiner's withdrawal of the previous rejections based on **Tomita et al.**

However, in the Office Action the Examiner rejected Claims 1 and 25 under 35 U.S.C. §102(b) as having been anticipated by **Farhadieh** (U.S. Patent No. 4,025,654). The Examiner rejected Claims 1 and 25-27 under 35 U.S.C. §103(a) as being unpatentable over **Petrus** (U.S. Patent No. 5,875,799) or Brown et al. (J. Clinical Pharmacy 1: 29-37 (1976)). The following remarks are addressed to these rejections.

Rejections under 35 U.S.C. §102(b)

Applicant respectfully traverses the rejections based on **Farhadieh**. That reference is entirely concerned with providing a water soluble version of the antibiotic chelocardin. The patent teaches that all the known soluble forms of chelocardin are chemically unstable and produce a product that rapidly breaks down. It is demonstrated that by making a mixture of chelocardin and sodium citrate dihydrate of between 1:0.2 and 1:2 by weight a stable soluble product is formed. That is, citrate prevents the break down of chelocardin. In this vein the patent teaches a composition of chelocardin containing at least 1% by weight citrate. Therefore, to the extent that chelocardin is an antibiotic, Claims 25 and 27 would appear to be anticipated. Those claims are now cancelled.

However, **Farhadieh** contains no teaching or suggestion that addition of citrate in any way enhances the effectiveness of chelocardin. On the other hand data presented in the instant application show enhancement of effectiveness and

do not deal with stability. The effectiveness (i.e., ability to kill or inhibit microorganisms) of a given concentration of antibiotic is show. In parallel the same concentration of antibiotic is enhanced by adding citrate. A common definition of enhancement is "To make greater, as in value, beauty, or effectiveness; augment." A method of enhancement results in a given amount of a compound producing a greater result. In **Farhadieh** there is no teaching of enhancement because the chelocardin decomposes in the usual solutions and does not decompose in the citrate solution meaning that the amount of chelocardin changes. One does not have a situation where the effectiveness of a fixed amount of compound is changed by the addition of citrate. Therefore, Applicant respectfully requests that the rejections of Claims 1 and 26 be withdrawn because the reference fails to teach the enhancement of effectiveness.

Rejection under 35 U.S.C. §103(a)

Applicant respectfully traverses the rejections based on **Petrus**. That reference teaches the effectiveness of zinc salts including zinc citrate. The patent teaches (see especially column 4) that zinc salts, including zinc citrate, are therapeutically effective in treating periodontal disease—especially with avoding the accumulation of plaque. Zinc is described as being "antimicrobial" but there is no teaching or suggestion that the citrate salt is more effective than any of the other zinc salts mentioned. In column 7 of the patent it is disclosed that antibiotics have been used as "other active agents" in combating periodontal disease. There is absolutely no teaching of a synergistic interaction between the zinc citrate and the antibiotic. Rather, the combination is simply envisioned as providing two rather than a single therapeutic agents. Since there is no teaching of synergism or enhancement of the additional therapeutic agent (e.g., antibiotic) by the primary therapeutic agent (e.g., zinc citrate), one of skill in the art could never derive the

method of the instant invention—namely enhancing an antibiotic by adding citrate—from the **Petrus** disclosure. Therefore, Applicant respectfully requests the Examiner to withdraw the rejections of Claims 1 and 26 based on **Petrus.**

The Examiner rejected the claims as being unpatentable under 35 U.S.C. §103(a) in view of a reference by Brown and Kayes. The Examiner presented an abstract of the reference and argued that "Brown teaches a process of combining ingredients consisting essentially of sodium citric acid salt with ampicillin[.]" Relevance of this reference to a composition has been mooted by the cancellation of Claims 25 and 27. Applicant has attached a complete copy of the Brown reference for the Examiner's information. From the complete reference it becomes clear that the reference is concerned with formulation of a liquid version of common solid drugs. In the case of ampicillin the reference discloses that stability of dissolved ampicillin is pH sensitive and shows a U shaped profile with a broad minimum between pH 4.5-6.0 (page 35, first compete paragraph). Consequently, the authors adjusted the pH to pH 6.15—outside of the unstable range—with sodium citrate. It is clear that sodium citrate was used as a simple pH buffer. No special properties are attributed to citrate. There is absolutely no teaching of enhancement of antibiotic effectiveness due to citrate. Nor would one of skill in the art employ 1% citrate because such a concentration would not produce the optimal pH. Because this reference neither teaches nor suggests that antibiotics can be enhanced by adding citrate, Applicant respectfully requests that the Examiner withdraw the rejections based on it.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner still finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles telephone number listed below to discuss the steps necessary for placing the application in condition for allowance.

You are hereby authorized to charge any fees due and refund any surplus fees to our Deposit Account No. 50-2567.

Respectfully submitted,

REED SMITH CROSBY HEAFEY

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By: _____

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Attachment: Complete copy of Brown and Kayes.